REMARKS

Claims 22, 32, 33, 36-41, 51, 55-61, 64-68 and 71-74 are pending and under consideration.

1. Rejections under 35 U.S.C. § 103

A. Claims 22, 32-33, 36-41, 51, 55-61, 64-68 and 71-74 are rejected under 35 U.S.C. § 103(a), allegedly, as obvious over EP 639373 (the '373 patent"), in combination with either U.S. Patent No. 5,049,388 to Knight *et al.* ("Knight"), or U.S. Patent No. 5,049,389 to Radhakrishnan ("Radhakrishnan"), or U.S. Patent No. 5,290,540 to Prince and Hemming ("Prince"); or *vice versa*. According to the Examiner, "[i]n the absence of showing unexpected results, it is deemed obvious to one of ordinary skill in the art to use an anti-septic agent and a wound healing promoting agent(encapsulated in liposomes) taught by [the '373 patent] to any part of the body including the respiratory tract . . ."

Applicants respectfully disagree with the Examiner's rejection. In order to not unduly burden the record, Applicants, while maintaining the arguments previously made in response to the Office Action mailed March 10, 2004, incorporate herein by reference those arguments and respond herein to particular comments made by the Examiner in order to advance the prosecution of the present application.

The Examiner states on page 3 of the Office Action mailed December 22, 2004 ("the Office Action") that "[the '373 patent] teaches the administration of the composition to mucous membranes." Further, on page 4 of the Office Action, the Examiner states:

> Applicant once again argues that skin or eye tissue in not equivalent to the tissue found in the lower respiratory tract. This argument has been addressed before. In essence, although the composition in [the '373 patent] is for external use, [the '373 patent] clearly teaches on page 2, lines 1-9 that the preparations are meant for application to the mucous membranes in humans and furthermore, [the '373 patent] is directed to the treatment of eye conditions.

In response, Applicants respectfully point out that the '373 Patent teaches, *inter alia*, the external application of liposomes containing povidone iodine, which external application includes application to the eye, which the Examiner will no doubt agree is on the outside of the body. A reference must be read in its entirety and when the '373 patent is read in its entirety it is clear that application of the disclosed compositions is only for external application, including application to the eye. Further, there is no teaching or suggestion that

"mucous membranes" or any other phrase in the '373 patent is meant to encompass the specialized tissue of the lower lung.

Further, the Examiner states on pages 4-5 of the Office Action that "[t]he safe nature and the effectiveness of the liposomes and the safe nature of the anti-microbial povidone iodine is obvious from the combined teachings of the references and hence one of ordinary skill in the art would be motivated to use the compositions containing PVP-iodine of [the '373 patent] by inhalation route taught by Knight or Radhakrishnan or Prince." However, Applicants point out that there is no teaching or suggestion in the '373 patent that liposomes containing PVP-iodine can be administered to the lower respiratory tract, which is different from the external mucosa (and the eye).[1] Applicants request that the Examiner provide a clear and particular showing that there is some motivation to combine the references rather than the general reasoning that since liposomes have been administered to the lung anything combined with liposomes can be administered to the lung. It is well settled law that identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. Rather to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). This showing of combinability must be "clear and particular". *In re Dembiczak*, 175 F.3d 994, 999; 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Examiner has not made this clear and particular showing. *See, also, Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569, 19 U.S.P.Q.2d 1241 (Fed. Cir. 1991) "We do not 'pick and choose among the individual elements of assorted prior art references to recreate the claimed invention,' but rather, we look for 'some teaching or suggestion in the references to support their use in the particular claimed combination.'"

With regard to the Examiner's statement on page 5 of the Office Action that "[i]t is interesting to note that in instant claim applicant recites 'mercury containing compound' and formaldehyde releasing compound'", Applicants note that such compounds are not recited in the pending claims.

[1]The Examiner is directed to page 11 of the Reply dated September 10, 2004 explaining that the tissue of the lower respiratory tract is quite different from the external mucosa and eye.

The Examiner states on pages 6-7 of the Office Action that "[t]hese arguments would have been persuasive if applicant has shown through in vivo studies, the safe and effectiveness of povidone iodine. However, instant specification does not contain any in vivo studies." Applicants are confused by the Examiner's statement because this appears to be reasoning on why the claimed invention would be not enabled, yet the Examiner has withdrawn the enablement rejection. Nevertheless, the present inventors have observed that application of liposomes containing povidone iodine does not harm ciliated lung cells as measured by the ability of the cilia to beat. The Examiner's attention is invited to International Patent Publication WO 99/60998, which is of record in the present application, and in particular to Test IV on pages 23-24 of the publication. As disclosed therein, when ciliated epithelium cells were exposed to 5% or 2.5% povidone iodine in solution, no ciliary activity was subsequently observed. However, when the cells were exposed to liposomes with 4.5% povidone iodine, no difference in ciliary activity was seen as compared to the control cells. Applicants respectfully submit that these results clearly show, in a relevant *in vitro* model, that application of PVP-iodine alone would be highly detrimental to ciliated lung cells *in vivo* whereas application of liposomes containing PVP-iodine would not harm the ciliated lung cells. Such data in combination with the known antiseptic effect of PVP-iodine is clearly predictive of the safe and effective administration of liposomes containing PVP-iodine to the lower respiratory tract to treat an infection.

In view of the foregoing, Applicants respectfully submit that this Section 103 rejection is in error and request its withdrawal.

B. Claims 22, 32-33, 36-41, 55-61, 64-68 and 71-74 are rejected under 35 U.S.C. § 103(a), allegedly, as obvious over EP 639373 (the '373 patent"), in combination with either U.S. Patent No. 5,049,388 to Knight *et al.* ("Knight"), or U.S. Patent No. 5,049,389 to Radhakrishnan ("Radhakrishnan"), or U.S. Patent No. 5,290,540 to Prince and Hemming ("Prince"); or *vice versa*, further in view of International Patent Publication WO 85/00112 ("International publication"). According to the Examiner, the International publication teaches the administration of vaporized povidone iodine to the nasal passages, and, thus, the International publication teaches that povidone iodine can be administered safely by inhalation, and thus, methods for treating an infection in the lower respiratory tract by administering liposomes containing povidone iodine are obvious.

Applicants respectfully disagree with the Examiner's rejection. In order to not unduly burden the record, Applicants, while maintaining the arguments previously made in response

to the Office Action mailed March 10, 2004, incorporate herein by reference those arguments and respond herein to particular comments of the Examiner in order to advance the prosecution of the present application.

The Examiner makes several statements on page 6 of the Office Action in finding that Applicants' arguments made previously in response to the same rejection are not persuasive. One such statement is that the present invention does not exclude heated air. Applicants do not understand the point the Examiner is trying to make and respectfully request that the Examiner provide further explanation. As Applicants have previously explained, the heated air component is as an important part of the methods described in the International publication as are the microbiocidal agents and that there is no indication that povidone iodine can be administered without heated air. Further, the Examiner states that the International publication teaches the safe administration of povidone iodine "internally"; however, Applicants respectfully submit that this statement is incorrect in view of a careful reading of the International publication. The International publication teaches that microbiocidal agents, including povidone iodine, can be administered by inhalation of a stream of heated air containing the agents to the nasal passages only. There is absolutely no teaching or suggestion that povidone iodine can be administered to any other part of the respiratory tract, much less the lower respiratory tract. No where in the International publication is any other site of administration taught or suggested.

The Examiner's statement that "it would be obvious to anyone that when a compound vapors are inhaled through the nose, those vapors would not just stop at the nose, but would get into the respiratory tract which according to applicant includes even trachea and applicant has not shown that to be otherwise", is pure speculation, which is an improper basis for a rejection. Applicants respectfully request that the Examiner provide a basis for such a statement, especially in view of the teaching of the International publication which is solely directed to the nasal passages.

Further, and regardless of whether the Examiner's statement that inhalation inevitably results in administration to the lower respiratory tract is factually correct or not, Applicants have previously set forth specific evidence in the prior art teaching that one of skill in the art would have been taught away from administering PVP-iodine to the lower respiratory tract. Further, and as explained above, Applicants themselves have shown that administration of PVP-iodine to ciliated lung cells *in vitro* damages such cells by destroying the ability of the cilia to beat. However, administration of liposomes containing PVP-iodine did not damage

such cells. See the discussion above with regard to International Patent Publication WO 99/60998, and in particular to Test IV on pages 23-24.

Therefore, for similar reasons as given above, the claimed methods are not rendered obvious by the '373 patent in combination with Knight, Radhakrishnan and Price, further in view of the International publication. Thus, Applicants respectfully request the withdrawal of this Section 103 rejection.

CONCLUSION

Applicants respectfully request that the above-made amendments and remarks of the present response be entered and made of record in the file history present application. Applicants submit that the presently pending claims meet all requirements for patentability and respectfully request allowance and action for issuance.

Applicants request that the Examiner call the undersigned at (212) 326-3921 if any questions or issues remain.

Respectfully submitted,

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Enclosures